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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/988,899	11/19/2001	Hendricus Renerus Jacobus Mattheus Hoogenboom	DX/003 CON	9170

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EXAMINER	
PONNALURI, PADMASHRI	
ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 12/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/988,899	HOOGENBOOM, HENDRICUS RENERUS JACOBUS M	
	Examiner	Art Unit	
	Padmashri Ponnaluri	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,11,12,15 and 16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,11,12,15 and 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/22/05 has been entered.

2. Claims 1-3, 11-12, 15-16 are currently pending and are being examined in this application.

Priority

3. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Europe on 5/18/99.

4. Receipt is acknowledged of papers submitted on 12/2/04 under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Claim Rejections

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claims 1-3, 11-12, 15-16 are rejected under 35 U.S.C. 102(a) as being anticipated by EP 844306 A1 (reference provided by applicants).

The instant claims briefly recite a library of vectors, wherein each vector comprising, a) first and second cloning region comprising unique restriction enzyme cleavage site, a ribosome binding site and a signal sequence, b) a polynucleotide encoding anchor region, c) a first and second variable antibody regions, and d) a polynucleotide encoding a tag.

EP 844306 A1 teaches methods for producing members of specific binding pairs. The reference teaches DNA encoding a genetically diverse population of specific binding pairs in recombinant host cells. The reference teaches that the recombinant genetic packages (refers to the vectors of the instant claims). The reference teaches a library of 10^{14} possible clones expressing the combination of H and L chain (refers to instant claims 3, 11-16) (e.g., see page 6). The reference vector comprises rbs at the 5' end of cloning regions, restriction enzyme sites and first and second cloning regions comprising Vh and Vl antibody fragments, gIII at the 3'end of the second cloning region (e.g., see figure 27). The reference teaches that the vector has a sequence encoding a C-terminal peptide tag for detection (reads on the instant claim tag) (i.e., see page 46).

The instant claim recites ' library of vectors, wherein each vector in the library has a member of a first variable polynucleotides encoding a first polypeptide, and a member of a second plurality of variable polynucleotides encoding a second polypeptide', which is interpreted as 'each vector has a first member of the polynucleotides, and a second member of the polynucleotides.' That is each vector has one single first polynucleotide sequence encoding a single first polypeptide, and a second single polynucleotide encoding a single polypeptide. The

reference teaches that both vH and vL chains cloned into the same vector, in which one of the chain is already known to have desired properties is kept fixed' which is interpreted as 'vector comprising first polyncucleotides encoding a first polypeptide, and a second polynucleotide encoding a second polypeptide.' In the reference the chain, which is already known to have desired properties has been selected from the combinatorial antibody library of either L chain or H chain. Thus, the first member or the second member is considered as variable.
Thus, the reference clearly anticipates the claimed invention.

7. Claims 1-3, 11-12, 15-16 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent 5,969,108 (McCafferty et al) (filing date Jan 1993).

The instant claims briefly recite a library of vectors comprising, a) first and second cloning region comprising unique restriction enzyme cleavage site, a ribosome binding site and a signal sequence, b) a polynucleotide encoding anchor region, c) a first and second variable antibody regions, and d) a polynucleotide encoding a tag.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

McCafferty et al teach methods for producing members of specific binding pairs. The reference teaches DNA encoding a genetically diverse population of specific binding pairs in

recombinant host cells. The reference teaches that the recombinant genetic packages (refers to the vectors of the instant claims). The reference teaches a library of 10^{14} possible clones expressing the combination of H and L chain (refers to instant claim 3) (e.g., see column 6). The reference teaches vectors (or genetic packages) comprising from 5' to 3', rbs-enzyme cleavage site, vH –rbs-enzyme cleavage site-vL-N' terminus of gene III (e.g., see figure 45). The reference teaches that the vector has a sequence encoding a C-terminal peptide tag for detection (i.e., see column 63, figure 26).

The instant claim recites ' library of vectors, wherein each vector in the library has a member of a first variable polynucleotides encoding a first polypeptide, and a member of a second plurality of variable polynucleotides encoding a second polypeptide', which is interpreted as 'each vector has a first member of the polynucleotides, and a second member of the polynucleotides.' That is each vector has one single first polynucleotide sequence encoding a single first polypeptide, and a second single polynucleotide encoding a single polypeptide. The reference teaches that both vH and vL chains cloned into the same vector, in which one of the chain is already known to have desired properties is kept fixed' which is interpreted as 'vector comprising first polyncucleotides encoding a first polypeptide, and a second polynucleotide encoding a second polypeptide.' In the reference the chain, which is already known to have desired properties has been selected from the combinatorial antibody library of either L chain or H chain. Thus, the first member or the second members are considered as variable.

Thus the reference clearly anticipates the claimed invention.

8. Claims 1-3, 11-16 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent 6,172,197 B1 (McCafferty et al)

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

McCafferty et al teach methods for producing members of specific binding pairs. The reference teaches DNA encoding a genetically diverse population of specific binding pairs in recombinant host cells. The reference teaches that the recombinant genetic packages (refers to the vectors of the instant claims). The reference teaches a library of 10^{14} possible clones expressing the combination of H and L chain (refers to instant claim 3) (e.g., see column 6). The reference teaches vectors (or genetic packages) comprising from 5' to 3', rbs-enzyme cleavage site, vH –rbs-enzyme cleavage site-vL-N' terminus of gene III (e.g., see figure 45). The reference teaches that the vector has a sequence encoding a C-terminal peptide tag for detection.

The instant claim recites ' library of vectors, wherein each vector in the library has a member of a first variable polynucleotides encoding a first polypeptide, and a member of a second plurality of variable polynucleotides encoding a second polypeptide', which is interpreted as 'each vector has a first member of the polynucleotides, and a second member of the polynucleotides.' That is each vector has one single first polynucleotide sequence encoding a single first polypeptide, and a second single polynucleotide encoding a single polypeptide. The

reference teaches that both vH and vL chains cloned into the same vector, in which one of the chain is already known to have desired properties is kept fixed' which is interpreted as 'vector comprising first polyncucleotides encoding a first polypeptide, and a second polynucleotide encoding a second polypeptide.' The reference teaches combinatorial libraries of both H chain and V chains. Thus, the reference teaches variants of first members and second members. In the reference the chain, which is already known to have desired properties has been selected from the combinatorial antibody library of either L chain or H chain. Thus, the first member or the second members are considered as variable. Thus the reference clearly anticipates the claimed invention.

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 1-3, 11-12, 15-16 are rejected under 35 U.S.C. 103(a) as being obvious over either US Patent 5,969,108 or US Patent 6,172,197.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

The instant claims briefly recite a library of vectors, wherein each vector comprising, a) First and second cloning region comprising unique restriction enzyme cleavage site, a ribosome binding site and a signal sequence, b) a polynucleotide encoding anchor region, c) a first and second variable antibody regions, and d) a polynucleotide encoding a tag.

McCafferty et al teach methods for producing members of specific binding pairs. The reference teaches DNA encoding a genetically diverse population of specific binding pairs in recombinant host cells. The reference teaches that the recombinant genetic packages (refers to

the vectors of the instant claims). The reference teaches a library of 10^{14} possible clones expressing the combination of H and L chain (refers to instant claim 3) (e.g., see column 6). The reference teaches vectors (or genetic packages) comprising from 5' to 3', rbs-enzyme cleavage site, vH –rbs-enzyme cleavage site-vL-N' terminus of gene III (e.g., see figure 45). The reference teaches that the vector has a sequence encoding a C-terminal peptide tag for detection. The instant claim recites ' library of vectors, wherein each vector in the library has a member of a first variable polynucleotides encoding a first polypeptide, and a member of a second plurality of variable polynucleotides encoding a second polypeptide', which is interpreted as 'each vector has a first member of the polynucleotides, and a second member of the polynucleotides.' That is each vector has one single first polynucleotide sequence encoding a single first polypeptide, and a second single polynucleotide encoding a single polypeptide. The reference teaches that both vH and vL chains cloned into the same vector, in which one of the chain is already known to have desired properties is kept fixed' which is interpreted as 'vector comprising first polyncucleotides encoding a first polypeptide, and a second polynucleotide encoding a second polypeptide.' In the reference the chain, which is already known to have desired properties has been selected from the combinatorial antibody library of either L chain or H chain. And further, the reference teaches in each vector one of the chain is already known to have desired properties, however in combinatorial library multiple such vectors would read on variable polynucleotide sequences as the instant claims. Thus, it would have been obvious to one skilled in the art to use the combinatorial approaches taught by the reference to clone different combinations of the first chain and second chain into the vectors, and methods of screening for functional Fab. A person skilled in the art would have been motivated to use the variable first member of polynucleotides

and variable second polynucleotides into the same vector, because such vectors will have more diversity and express polyclonal antibodies.

Response to Arguments

12. Applicant's arguments filed on 9/22/05, regarding the art rejections over EP 0844306 A1, US Patents 6,172,197 B1, 5,969,108 have been fully considered but they are not persuasive.

Applicants traverse the rejection. Applicants assert hat the instant claims recite a plurality of vectors, which comprise a first and second plurality of variable polynucleotides, and the '306 application does not teach any such vectors. Further applicants refer to the fourth approach, and argue that the '306 application fourth approach does not teach a library of vectors characterized by two plurality of polynucleotides. And further assert that the reference teaches in the vector one of the chains is kept fixed.

Applicant's arguments have been fully considered and are not persuasive, because the reference teaches combinatorial libraries of antibody polypeptides, and the reference teaches both chains (vH and vL) are cloned into the same vector, in which the first chain is already known to have desired property. In the reference 'the chain is already known to have desired property' does not mean that the chain does not have variable sequence. The reference teaches methods of making combinatorial libraries of either heavy chain or light chain, and methods of screening the combinatorial antibody libraries. Thus, it would have been obvious to one skilled in the art at the time the invention was made to use the different combinatorial libraries of antibody heavy chain or light chain and clone the different libraries into the same vector and screen for diverse combinations of antibody heavy chain and light chain. Thus, the rejections of record have been maintained for the reasons of record.

Conclusion

13. No claims are allowed

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padmashri Ponnaluri whose telephone number is 571-272-0809. The examiner can normally be reached on Monday through Friday between 7 AM and 3.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Padmashri Ponnaluri
Primary Examiner
Art Unit 1639

20 December 2005